AMENDMENTS TO THE CLAIMS:

This listing of claims will replace prior versions and listings of claims in the application:

Listing of claims:

Claim 6 has been amended as follows: Underlines indicate insertions and ~~strikeouts~~ indicate deletions.

1. (withdrawn) A method for obtaining a Neprilysin-like (NEP-like) metallopeptidase which comprises the following steps:
   - selecting a primer in C-terminus of the His-Glu-Xaa-Xaa-His (where Xaa represents any amino acid) with a degenerate nucleotide sequence complementary to at least the Gly-Glu-Asn-Ile-Ala-Asp amino acid sequence of known NEP-like metallopeptidases with sufficient binding capacity;
   - selecting a primer in N-terminus of the His-Glu-Xaa-Xaa-His (where Xaa represents any amino acid) with a degenerate nucleotide sequence complementary to a conserved amino acid sequence with preferably 80% homology with known NEP-like metallopeptidases and sufficient binding capacity;
   - contacting said primer with tissue nucleic acids to yield PCR products;
   - selecting said PCR products that contain the His-Glu-Xaa-Xaa-His motif; and
   - completing the sequence of said selected PCR products with standard methods.

2. (withdrawn) A metallopeptidase sharing about 80% homology with the amino acid sequence shown in Figure 3.

3. (withdrawn) A metallopeptidase which is soluble sharing about 80% homology with the amino acid sequence in C-terminus of the furin site shown in Figure 3.

4. (withdrawn) A metallopeptidase which is soluble sharing about 80% homology with the amino acid sequence shown in Figure 3 and with an enzymatic activity capable of degradation of known Neprilysin substrates, preferably Tyrosyl-[3,5-^{3}H1)(D-Ala$_2$)-Leu$_5$-enkephalin and bradykinin.

5. (withdrawn) A composition comprising a metallopeptidase as defined in claim 2.

6. (Currently amended) An isolated nucleic acid ~~encoding a NEP-like (NL) metallopeptidase~~ comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence encoding a metallopeptidase having at least about 77% identity with the complete amino acid sequence ~~in Figure~~of SEQ ID NO: 13 ~~3~~;

(b) a nucleotide sequence encoding a metallopeptidase having at least about 77% identity with the complete amino acid sequence ~~in Figure 4~~of SEQ ID NO: 15;

(c) the nucleotide sequence of SEQ ID NO: 12~~set forth in Figure 3~~;

(d) the nucleotide sequence of SEQ ID NO: 14~~set forth in Figure 4~~;

(e) a nucleotide sequence encoding a metallopeptidase having at least about 77% identity with the complete amino acid sequence of SEQ ID NO: 15 and having amino acids 1 to 63 of SEQ ID NO: 13;

(f) a nucleotide sequence encoding a N-terminal fragment of a metallopeptidase constituted of amino acids 1 to 63 of SEQ ID NO: 13;

(g) a nucleotide sequence encoding a N-terminal fragment of a metallopeptidase and constituted of nucleotides 332 to 520 of SEQ ID NO: 12; and

(~~e~~h) a nucleotide sequence completely complementary to any of the nucleotide sequences in (a), (b), (c), (d), (e), (f) and (~~d~~g); ~~and~~

(~~f~~i) a nucleotide sequence encoding a metallopeptidase which hybridizes under high stringency conditions to any of the nucleotide sequences in (a), (b), (c), (d), (e), (f), (g) and (h) ~~and (e)~~, wherein the high stringency conditions

comprise: pre-hybridization and hybridization in 6XSSC, 5XDenhardt's reagent, 0.5% SDS and 100mg/ml of denatured fragmented salmon sperm DNA at 68°C; and washes in 2XSSC and 0.5% SDS at room temperature for 10 min; in 2XSSC and 0.1% SDS at room temperature for 10 min; and in 0.1XSSC and 0.5% SDS at 65°C three times for 5 minutes.

7. (withdrawn) An antibody directed against a metallopeptidase as defined in claim 2.

8. (withdrawn) A method for obtaining a substrate of a metallopeptidase as defined in claim 2, which comprises the steps of:
-- contacting said metallopeptidase with a molecule or extract; and
-- assaying the resulting solution for a decrease in said molecule or extract, when compared with the same but in absence of said metallopeptidase, as an indication of the presence of said substrate.

9. (withdrawn) A method for obtaining an inhibitor of a metallopeptidase as defined in claim 2, which comprises the steps of:
-- contacting said metallopeptidase with a molecule or extract in the presence of a substrate selected known NEP substrates, preferably Tyrosyl-[3,5-^{3}H1)(D-Ala$_2$)-Leu$_5$-enkephalin and bradykinin; and
-- assaying the resulting solution for an increase in said substrate, when compared with the same but in absence of said metallopeptidase, as an indication of the presence of said inhibitor.

10. (withdrawn) An inhibitor obtained from the method of claim 9.

11. (withdrawn) The use of a known NEP inhibitor or an inhibitor as defined in claim 10 to control the enzymatic activity of a metallopeptidase as defined above.

12. (withdrawn) The use of a known NEP inhibitor or an inhibitor as defined in claim 10 to manage disease relating to the physiological status of the

cardiovascular system, the central nervous system, the spleen, the liver, the kidney, the male reproductive system or the maturation of spermatozoa.

13. (withdrawn) The use of a metallopeptidase as defined in claim 2 to manage disease relating to the physiological status of the cardiovascular system, the central nervous system, the spleen, the liver, the kidney, the male reproductive system or the maturation of spermatozoa.

14. (cancelled)

15. (withdrawn) A method for producing a soluble form of a protein, polypeptide or part thereof which comprises:
- obtaining nucleic acids encoding said protein, polypeptide or part thereof;
- fusing said nucleic acids in phase with an N-terminal fragment wherein said N-terminal fragment comprises a cleavable furin-like site located in C-terminus past the transmembrane region or is an N-terminal part as defined in claim 14;
- having the fused nucleic acids to be expressed in a host cell which expresses or is made to express furin in the presence of a culture medium; and
- recovering said soluble form in the culture medium.

16. (withdrawn) A protein, polypeptide or part thereof produced by the method defined in claim 15, wherein said protein, polypeptide or part thereof is a metallopeptidase sharing about 80% homology with the region in C-terminus of the putative furin site of the amino acid sequence shown in Figure 4.

17. (withdrawn) A metallopeptidase sharing about 80% homology with the region in C-terminus of the putative furin site of the amino acid sequence shown in Figure 4.

18. (withdrawn) A metallopeptidase sharing about 80% homology with the region in C-terminus of the putative furin site of the amino acid sequence shown in Figure 4 and with an enzymatic activity capable of degradation of known NEP

substrates, preferably Tyrosyl-[3,5-^{3}H1)(D-Ala$_2$)-Leu$_5$-enkephalin and bradykinin.

19. (withdrawn) A composition comprising a metallopeptidase as defined in claim 16.

20. (withdrawn) A nucleic acid encoding a metallopeptidase as defined in claim 16.

21. (withdrawn) An antibody directed against a metallopeptidase as defined in claim 16.

22. (withdrawn) A method for obtaining a substrate of a metallopeptidase as defined in claim18, which comprises the steps of:
-- contacting said metallopeptidase with a molecule or extract; and
-- assaying the resulting solution for a decrease in said molecule or extract, when compared with the same but in absence of said metallopeptidase, as an indication of the presence of said substrate.

23. (withdrawn) A method for obtaining an inhibitor of a metallopeptidase as defined in claim16, which comprises the steps of:
-- contacting said metallopeptidase with a molecule or extract in the presence of a substrate selected from known NEP substrates or a protein, polypeptide or part thereof produced by the method of claim 15, preferably Tyrosyl-[3,5-^{3}H1)(D-Ala$_2$)-Leu$_5$-enkephalin and bradykinin; and
-- assaying the resulting solution for an increase in said substrate, when compared with the same but in absence of said metallopeptidase, as an indication of the presence of said inhibitor.

24. (withdrawn) An inhibitor obtained from the method of claim 23.

25. (withdrawn) The use of a known NEP inhibitor or an inhibitor as defined in claim 24 to control the enzymatic activity of a metallopeptidase as defined above in claim 16.

26. (withdrawn) The use of a known NEP inhibitor or an inhibitor as defined in claim 24 to manage disease relating to the physiological status of the cardiovascular system, the central nervous system, the spleen, the liver, the kidney, the male reproductive system or the maturation of spermatozoa.

27. (withdrawn) The use of a metallopeptidase as defined in claim 16 to manage disease relating to the physiological status of the cardiovascular system, the central nervous system, the spleen, the liver, the kidney, the male reproductive system or the maturation of spermatozoa.

28. (withdrawn) A method as defined in claim 15, wherein said protein, polypeptide or part thereof is beta-endorphin.

29. (cancelled)

30. (withdrawn) A metallopeptidase sharing about 80% homology with the amino acid sequence located in the C-terminus of the predicted transmembrane domain of the amino acid sequence shown in Figure 5 which has been produced by the method of claim 15, by fusing in frame a cleavable signal peptide in N-terminus of said amino acid sequence or by transforming said predicted transmembrane domain into a cleavable signal peptide.

31. (withdrawn) A composition comprising a metallopeptidase as defined in claim 30.

32. (withdrawn) An antibody directed against a metallopeptidase as defined in claim 30.

33. (withdrawn) A method for obtaining a substrate of a metallopeptidase as defined in claim 30, which metallopeptidase shares about 80% homology with the C-terminal region of the predicted transmembrane domain of the amino acid sequence shown in Figure 5, comprising the steps of:
-- contacting said metallopeptidase with a molecule or extract; and

-- assaying the resulting solution for a decrease in said molecule or extract, when compared with the same but in absence of said metallopeptidase, as an indication of the presence of said substrate.

34. (withdrawn) A method for obtaining an inhibitor of a metallopeptidase sharing about 80% homology with the C-terminal region of the predicted transmembrane domain of the amino acid sequence shown in Figure 5, which comprises the steps of:
-- contacting said metallopeptidase with a molecule or extract in the presence of a substrate produced by the method of claim 33; and
-- assaying the resulting solution for an increase in said substrate, when compared with the same but in absence of said metallopeptidase, as an indication of the presence of said inhibitor.

35. (withdrawn) An inhibitor obtained by the method of claim 34.

36. (withdrawn) The use of an inhibitor as defined in claim 35 to control the enzymatic activity of the metallopeptidase sharing about 80% homology with the C-terminal region of the predicted transmembrane domain of the amino acid sequence shown in Figure 5.

37. (withdrawn) The use of an inhibitor as defined in claim 35 to manage disease relating to the physiological status of the central nervous system, the spleen or the bones.

38. (withdrawn) The use of a metallopeptidase as defined in claim 30 to manage disease relating to the physiological status of the cardiovascular system, the central nervous system, the spleen or the bones.

39. (previously presented) A recombinant vector comprising an isolated nucleotide sequence of claim 6.

40. (currently amended) A recombinant host cell capable of expressing a ~~NEP-Like protein~~metallopeptidase, polypeptide or part thereof comprising the vector of claim 39.

41. (new) An isolated nucleic acid as recited in claim 6, wherein the nucleotide sequence encodes a metallopeptidase having at least about 77% identity with the complete amino acid sequence of SEQ ID NO: 13.

42. (new) A recombinant vector comprising an isolated nucleotide sequence of claim 41.

43. (new) A recombinant host cell capable of expressing a metallopeptidase, polypeptide or part thereof comprising the vector of claim 42.

~~42.~~44. (new) An isolated nucleic acid as recited in claim 6, wherein the nucleotide sequence encodes a metallopeptidase having at least about 77% identity with the complete amino acid sequence of SEQ ID NO: 15.

45. (new) A recombinant vector comprising an isolated nucleotide sequence of claim 43.

46. (new) A recombinant host cell capable of expressing a metallopeptidase, polypeptide or part thereof comprising the vector of claim 45.

~~43.~~47. (new) An isolated nucleic acid as recited in claim 6, wherein the nucleotide has the sequence of SEQ ID NO: 12.

48. (new) A recombinant vector comprising an isolated nucleotide sequence of claim 47.

49. (new) A recombinant host cell capable of expressing a metallopeptidase, polypeptide or part thereof comprising the vector of claim 48.

~~44.~~50. (new) An isolated nucleic acid as recited in claim 6, wherein the nucleotide has the sequence of SEQ ID NO: 14.

51. (new) A recombinant vector comprising an isolated nucleotide sequence of claim 50.

52. (new) A recombinant host cell capable of expressing a metallopeptidase, polypeptide or part thereof comprising the vector of claim 51.

~~45.~~53. (new) An isolated nucleic acid as recited in claim 6, wherein the nucleotide sequence encodes a metallopeptidase having at least about 77% identity with the complete amino acid sequence of SEQ ID NO: 15 and having amino acids 1 to 63 of SEQ ID NO: 13.

54. (new) A recombinant vector comprising an isolated nucleotide sequence of claim 53.

55. (new) A recombinant host cell capable of expressing a metallopeptidase, polypeptide or part thereof comprising the vector of claim 54.

~~46.~~56. (new) An isolated nucleic acid as recited in claim 6, wherein the nucleotide sequence encodes a N-terminal fragment of a metallopeptidase and is constituted of a polypeptide having amino acids 1 to 63 of SEQ ID NO: 13.

57. (new) A recombinant vector comprising an isolated nucleotide sequence of claim 56.

58. (new) A recombinant host cell capable of expressing a metallopeptidase, polypeptide or part thereof comprising the vector of claim 57.

~~47.~~59. (new) An isolated nucleic acid as recited in claim 6, wherein the nucleotide sequence encodes a N-terminal fragment of a metallopeptidase and is constituted of a polynucleotide having nucleotides 332 to 520 of SEQ ID NO: 12.

60. (new) A recombinant vector comprising an isolated nucleotide sequence of claim 59.

61. (new) A recombinant host cell capable of expressing a metallopeptidase, polypeptide or part thereof comprising the vector of claim 60.